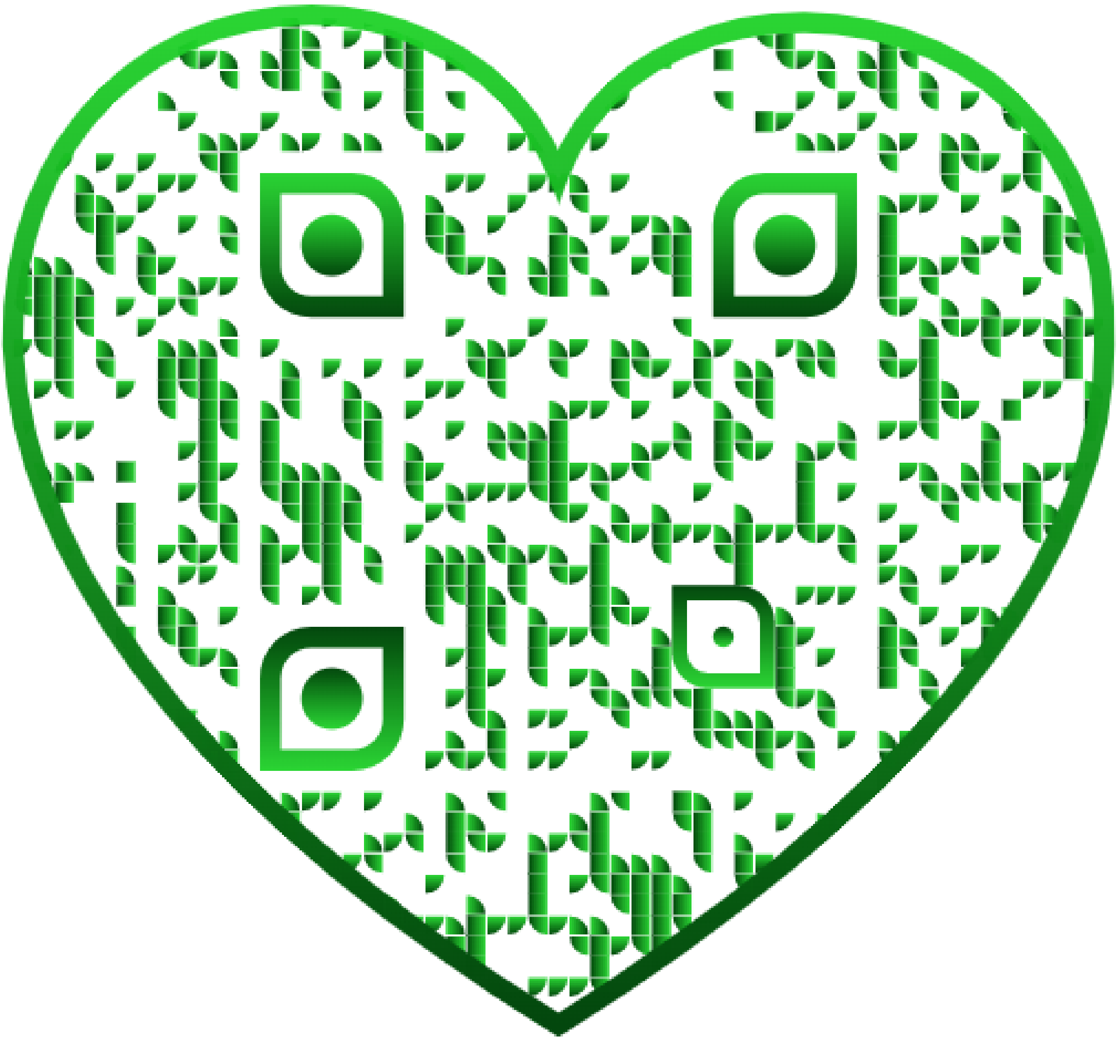
ENDOCRINE
SYSTEM



⊛. major organs of endocrine system
①. hypothalamus
② -pituitary gland
③. Thyroid and parathyroid glands
④ - Adrenal glands
⑤- pancreas
Gonads ⑥- Testes in male ~~and~~ ⑦. ovaries in female

1

التاريخ / / ٢٠١ الموضوع :

* Endocrine system *.

* the regulation of all Function of the body are Controlling by two systems
1- Central Nervous system.
2- Endocrine System.

Glands
- * the exocrine system (has duct)
  ex:- salivary and sweat gland and mammary gland
- * the endocrine system (has no duct) → blood

ex:- 1- pituitary gland.
2- thyroid and parathyroid gland.
3- adrenal gland.
4- testis
5- ovary
6- pancrease
7- hypothalamus.
8- liver, and kidney.

* all endocrine gland are pure gland Except Kidney and liver

ليس لها أي وظيفة آخرى غير الافراز

* hypothalamus also organ & endocrine gland.
* lung, heart also 〃 〃 〃 〃

*إذا انضربت الـhypothalamus كاملة قد يتوفى الإنسان

2

* hypothalamus gland :-

- it secretes 9 hormones , 7 hormones of them will transport to ant. pituitary gland. (this hormone in ant. pituitary will Controlling the most endocrine gland in the body)

* the hormones which secreted from hypothalamus :-

1- Antidiuretic hormone (ADH)
2- oxytocin
3- growth releasing hormone.
4- growth inhibiting hormone.
5- prolactin releasing hormone.
6- prolactin inhibiting hormone.
7- Corticotropin releasing hormone.
8- Thyrotropin releasing hormone.
9- Gonadotropin releasing hormone.

GHRH
↓
A.P
↓
GH

TRH
↓ act on :-
Ant. pituitary
↓ secret :-
TSH
↓ act on
thyroid gland
↓ secret.
T_4 & T_3

1- * Antidiuretic hormone (ADH) * تفرز في حالة → dehydration

- Storage in post. pituitary gland.
- it Decrease urine by increase reabsorption of water.

* N.B :-

- the oxytocin and Antidiuretic hormone secreted from hypothalamus and Storage in post. pituitary gland.

2- * Oxytocin *.

- Contraction of uterus. (in pregnant women)
- ejection of the milk.
  (by squeezing the mammary gland)

- it is found in both (male and femal)
  ذكر
  Contraction of secondary sex organ
  (help in transport of sperm)

- also storage in post. pituitary gland.

* pituitary gland :-

عبارة عن ← 1- post. pituitary gland. ← storage تخزين and Relase
Nervous organ not secreting any hormones
ما تفرز أي هرمون
عبارة عن nervous organ

- Storage of oxytocin and ADH. (Releas).
(إطلاق)

2- Ant. pituitary gland
- it serect 7 hormones :-
1- Thyroid stimulating hormone. (TSH)
2- Growth hormone (GH)
3- prolactin (PRL)
4- Luteinizing hormone (LH)
5- Follicle - stimulating hormone (FSH)
6- Adrenocorticotropic hormone (ACTH)
7- Beta lipotropin (B-LPH). → with unknown function

TRH
↓
A.P
↓
TSH
↓
T_4 T_3 ← Thyroid

GHRH
↓
A.P
↓
GH

* N.B :-

- FSH and LH → found in Both (male and Female)

FSH → in female growth of follicle

FSH ↓ help in Spermatogenisis in male

LH → in female rapture and ovulation الإباضة

LH → synthesis of testesteron.

* prolactin *

- Formation of the milk.
- Found in Both sex (Male and female).
- in lactation state the prolacting hormone increase.
- prolactin in → male 8-9 nano gram.
  → female. 23-24 nano gram.
- increase prolactine hormone in male will Causes
  1- Infertility
  2- hypogonadism
- increase prolactin hormone in female will Causes
  1- disorder in menstrual cycle.
  2- Can't pregnant.

But if the prolactin increase to 100 ng or above ⇒ (Malignancy or tumor)

* البرولاكتين من الهرمونات التي تزيد أثناء الـ Stress ،

* أثناء الحمل يبدأ يرتفع البرولاكتين من الشهر الخامس طبيعياً .

الى 35 أو 40

تكيس المبيض
@ ovarian cyst → علامات إذا كان مزمن → اسوداد في الإبط
↘ يمرض المرأة ماتخلف
علامة
- يزيد عنده الاندروجين
- يتساقط شعر المرأة
- لخبطة في الدورة الشهرية
- ظهور الشعر في الجسم كامل

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* يرتفع الـ prolactin أثناء الحمل والسبب في الرفع هو هرمون الأستروجين (estrogen).

بالرغم من ارتفاع الـ prolactin إلا إنه لا يتم إدرار الحليب في فترة الحمل ؟

والسبب في ذلك هو أن الـ (estrogen) الموجود في جسم المرأة بنسبة عالية يعمل ارتباط مع receptor ويعمل لها (Block) الموجودة في الـ mammary gland .

* حبوب منع الحمل تكون
→ estrogen
→ progestron ← ضعيف (أضعف من estrogen).
→ estrogen & progestron .

* ممنوع للمرأة المرضعة استخدام الـ estrogen كمانع حمل لذلك تستخدم (progestron).

* Thyroid gland :→
1- Thyroxin (T_4) ⎤ → the same function.
2- Triiodothyronin (T_3) ⎦
3- Calcitonin. → ↓ Ca^{+2} absorption from blood to bone ← ↓ Ca^{+2} في blood ويأخذه إلى العظام ويجعلها قوية
4- Reverse T_3 → Storage.

* Para thyroid gland :-
1- Para thyroid hormone.
↑ Ca^{+2} absorption. From bone to blood
ويصبح الـ bone هش فيسبب ← osteoporosis هشاشة العظام

- في الحالة المرضية التي فيها هشاشة العظام يعني زيادة هرمون parathyroid hormone.

ⓐ في الـ hypothalamus الاسم الثاني لـ Somatostatine هو G.H. inhibiting hormon

ⓑ- الاندروجين تفرز بنسبة متساوية عند الرجل والمرأة من adrenal gland بنفس الكمية لكن عند الرجل

الـ Testes تفرز هرمون Testosteron وهو نوع من الاندروجين هرمون لذلك الاندروجين عند الرجل أكثر من المرأة

ⓒ- وظيفة الاندروجين عند المرأة اظهار الشعر في ← axilla ← pubic

★ هرمون التستستيرون نوع من أنواع الـ androgen

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الموضوع :　　　　　　التاريخ　/　/　٢٠١

- دائما somatostatine يعمل inhibition
- الاسم الثاني له G.H. inhibiting h.

* pancrease (Mixed gland):- →

1- Insulin

2- glucagon ← دائما يعمل inhibition

4- Somatostatine ←تفرز من D-cell ← الى توجد في:
① - pancrease
② - hypothalamus
③ - stomach
④ - small intestine

5- pancreatic Poly peptide

* Adrenal gland :-

(مهم جدا)
- تكلم عن وظائف الـ sympathetic هي نفس وظائف الـ

Cortex (about 30-40 hormones)	Medulla
1- Cortisol	1- Adrenaline
2- Aldosterone	2- nor-adrenaline
3- Androgen. (as dihydroepiandrosterone).	3- Dopamine →
4- Small amount of estrogen.	

* يستخدم في علاج الـ Cardiogenic shock لان هبوط الضغط في هذه الحالة سببه هو heart فعمل الـ Dopamine هو زيادة الـ contractility الـ heart. مما يؤدي الى رفع الضغط.

* Testes :-

1- Testosterone. → ↓ FSH

2- Inhibin ⇒ from sertoli cell (nurse cell)

3- Small amount of estrogen (with unknown Function)

ورم في الخصيتين عند المرأة التي تفرز الاندروجين لاحظ ظهور الشعر عند المرأة

* ovaries :-

1- Estrogen

2- progestrone

3- Inhibin ⇒ (↓ FSH) from granulosa cell

4. Relaxin ⇒ Relaxation of pelvic joint (in delivery) ← يفرز وقت الولادة

5- Small amount of testosterone ⇒ with unknown Function)

*أقرب مادة مشابهة للهرمونات هي ,الانزيمات

* Hormones :- It's a chemical substance secreted into the blood stream by endocrine gland to act on the distance organs called effectors organs.

مهمة * properties of hormones :-

1- They are secreted in very small amount → (active form)

ex:- Cortisol hormone found in blood in small amount, but during stress it will increas.

* the hormone connect with plasma protein * to prevent loss of hormone with urine after filtration.

2- Not act in gland secreting them.

ex:- Thyroid hormone act in all body except thyroid gland. (pure hormone).

ex:- active form of vit. D_3 :- it's vitamine, Because It act in gland which secreted it (kidney)

أيضاً يعتبر هرمون

3- hormones may act on specific effectors organs, OR may act on the body as whole.

ex:- adrenaline.

ex:- growth hormone act in all body except Brain.

*يسؤل عن لو Brain ـه Thyroid hormone

ex:- 1- Calcitonin hormone.
2- parathyroid hormone.
3- Sex hormone.
↳ this act in specific organs.

4- Stimuli that release a certain hormone, Inhibite the secretion of other hormone.

* hormone has related with growth:
1- growth hormone.
2- thyroid "
3- sex "
4- Insuline "
5- Cortisol "

ex:- hyperglycemia.
Stimulation of insulin.
& Inhibition of glucagon.

ex:- hyper calcemia
Stimulation of Calcitonine hormone
& Inhibition of parathyroid hormone.

* ↓ Ca^{+2} (osteoporosis) in female :- ← الأكثر عرضة
1- pregnancy
2- lactation.
3- Malnutrition

* في حالات يكون الشخص عنده هشاشة عظام ولكن عند فحص ال Ca^{+} تكون نسبة عالية وذلك بسبب (hyperparathyrodism) يعمل على سحب ال Ca^{+2} من bone إلى ال Blood وهذه الحالة هي أسوأ هشاشة عظام أبسط حركة تؤدي إلى كسر العظام.

5- Some hormones are secreted in relatively inactive form then they are converted in tissue to more active hormone.

ex:- testosterone → active ,but dihydrotestosterone is more active.

ex: T3 & T4 → active but
T3 is more active and rapid onset.
T3 → secreted in 4 Mg.
T4 → secreted in 80 Mg., when reach to tissue it will transform to T3.

* Types of hormones :→

1- proteins hormone

all hormones are protein hormones except

1- Estrogen
2- progestron
3- Androgen
4- testosterone
5- active form of vit. D3
6- aldosterone
7- Cortisol.

2- Steroids hormone

1- Adrenal Cortex hormone ←
  - Androgen
  - Cortisol
  - aldosterone.
2- Sex hormone ←
  - Astrogen
  - progestrone.
  - testosterone.
3- active form of Vit. D3

* Synthesis of hormone :-

1- protein hormone
in Rough endoplasmic reticulum.

2- Steroid hormone
in Smooth endoplasmic reticulum and Mitochondria.

* Release of hormones.

1- protein hormone
- Released by exocytosis, because it has high Molecular weight

2- Steroid hormone and thyroxin.
- Released by passive diffusion, because it has low Molecular weight.

* hormonal receptors :-

1- in the cell membrane of target cell
2- in side the target cell (in cytoplasm)
3- " " " " " (in nucleus)

* the hormonal receptor are dynamic structure (increase and decrease)
ممكن تزيد وممكن تنقص

* N.B :-

* Each hormone has specific receptor.

*The regulation of hormonal receptors is 2 types :-

1- Up regulation :-
(↑ increase the number of receptor during decrease the hormone).

2- Down regulation :-
(↑ increase hormone lead to ↓decrease the number of receptor).

* The hormone and number of Receptor has Inversly proportional :)

* Mechanism of action of hormone *

1- protein hormone :-
- by activation of enzyme system of cell. (c AMP)

2- Steroid hormone & thyroxin :-
by activation of genes of cell.

* Types of second messengers :-

1- C AMP ⇒ هنا المطلوب
2- C GMP. ⇒ such ANP & photoreceptor
3- Calcium ions (Calmodulin system)
4- Membrane phospholipids breakdown products :-
  a-inositol triphosphate (IP_3)
  b-Diacylglycerol (DAG) ⇒ ADH V_1

* Mechanism of protein hormones :-

1- Binding of hormone (first messenger) with the receptor which found in the cell membrane.
2- activation of receptor causes activation for G protein (which consist of 3 subunit $\alpha, \beta \& \gamma$)
3- Separation of subunit of G-protein, and α subunit (the largest subunit) causes activation for enzyme called adenylyl cyclase by binding to it.
4- the ATP will convert to cAMP by adenylyl cyclase. Causes the formation of second messenger (cAMP).
5- occur cell reseponce according to the function of hormone.

* N.B.

* الـ second messenger ، كل هرمون يكون second messenger خاص فيه
له نفس صفات الهرمون يقوم بنفس عمل الهرمون الذي كونه ، لأن الهرمون حجمه
كبير ولا يستطيع الدخول إلى داخل الخلية

*الأدرينالين و النورأدرينالين يشتغل على Receptors (α_1, α_2, B_1, B_2, B_3) 13

الموضوع : *الدوبامين يشتغل على Receptor (D_1, D_2, D_3, D_4, D_5) / / ٢٠١

* Most of hormones act with increase c AMP Except * Some hormones act with decrease c AMP ex:-

1- Somatostatine.
2- α_2 (Adrenaline & nor adrenaline)
3- Dopamine (D_2, D_3, D_4).

⇓

⇐

⇒

*Catecholamine hormone act in 3 ways:-

1- β by increase c AMP.
2- α_2 by decrease c AMP:
3- α_1 by Inositol triphosphate (IP_3)
↓ يعمل على زيادة نسبة Ca^{+2}.

*FSH & LH are protein hormone.

* Mechanism of action of Steroid hormones :-
(Steroid hormone & thyroxin)

(Steroid hormone made of Cholesterol and lipid soluble Substance).

1- the steroid hormone when reach to target cell, it will pass By simple diffusion (Because it's lipid soluble Substance)

2- in cytoplasm, the hormone Combined with Cytoplasmic receptor to Form hormone receptor Complex, which decrease in size, to enter the nucleus by pores.

3- in the nucleus the hormone receptor complex Combined with DNA to transcription of DNA to Form mRNA.

4- the m-RNA will Form in large amount, then exit From nucleus to cytoplasm.

5- in Cytoplasm the m-RNA goes to Ribosome. to synthesis protein.

6- each protein does Function of hormone's Functions.

* Mechanism of action of thyroxin :-
(thyroxin is protein hormone).

1- thyroxin Cross cell membrane directly to nucleus, in nucleus it Compind with nuclear receptor to Form hormone receptor Complex.

2- the hormone receptor Complex Combined with DNA, to transcription of DNA to m-RNA.

3- m-RNA exit nucleus to Cytoplam (ribosome)

4- the ribosome will form protein &(and) each protein dose Function of hormone's Function

pituitary gland (hypophysis)

- it's small gland, but called the master gland, because it regulate most of gland which found in body.

* it divided to :-
  1. anterior lobe. (adenohypophysis)
  2. Posterior lobe. (neurohypophysis)
  3. intermediate lobe.

سؤال ⇐ * the Connection btw hypothalamus and pituitary gland :-

1- Vascular :- Btw hypothalamus and ant. lobe of pituitary gland.

2- Nervous :- Btw hypothalamus and post. lobe of Pituitary gland.

∴ * the vessel which Connect with 2 Capillary is Called portal

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*** First : Vascular Connection :-**

1- Btw hypothalamus and ant. lobe of pituitary.

* Function of this Connection is transport of Seven hormones :-

1- Corticotropin - releasing hormone
2- Thyrotropin - releasing hormone.
3- Growth hormone - releasing hormone.
4- Growth hormone - inhibiting hormone. Somatostatin
5- prolactine // releasing //
6- prolactine // inhibiting // (= Dopamine)
7- Gonadotropin - releasing hormone

* the Superior hypophysial artery when enter to hypothalamus, it divided to primary Capillary plexuses

* the primary Capillary plexus when exit from hypothalamus, it will Connect with each other again to form hypothalamic-hypophysial portal vessels

* the portal vessels when enter to ant. pituitary gland, it will divid to secondary Capillary Plexus (Sinuses).

*** N.B :-**

- Primary Capillary plexus take hormones from hypothalamus.
- secondary Capillary plexus give hormones to ant. pituitary gland.

*أكبر عدد من Nuclei فيال Brain موجودة فيا ال hypothalamus.

الموضوع : التاريخ / / ٢٠١

*Second :- Nervous Connection.

1- Connect Btw hypothalamus and post. pituitary gland.

* Supraoptic nucleus :-

secrete ADH in 80-90%. ⇐ مهمة.

secrete oxytocin in 20-10%. ⇐ للمعلومة فقط.

* Supraoptic nucleus secrete oxytocin (✗) ⇐ لو كانت سؤال امتحان فقط هذه النسبة.

*paraventricular nucleus :-

secrete oxytocin in 80-90%. ⇐ مهمة

- Secrete ADH in 10-20%. ⇐ معلومة

* the oxytocin and ADH secrete from hypothalamus and Storage in post. lobe of pituitary gland.

(the hormones)* transport from hypothalamus the post. pituitary gland by hypothalamic hypophysial tract ⇒ (nervous)

* Ant. pituitary gland *

- it secrete 7 hormone

1- polypeptide hormones :-
    - a- Adrenocorticotropic hormone (ACTH)
    - b- prolactin (PRL).
    - c- Growth hormone (GH).
    - d- Beta lipotropin. (B-LPH).

2- Glycoprotein hormone :-
    - a- Thyroid stimulating hormone. (TSH)
    - b- Follicle stimulating hormone (FSH)
    - c- Luteinizing hormone (LH).

مهمة جداً ⟸ * Regulation of adenohypophyseal Function :-

1- Hypothalamic Controling :-

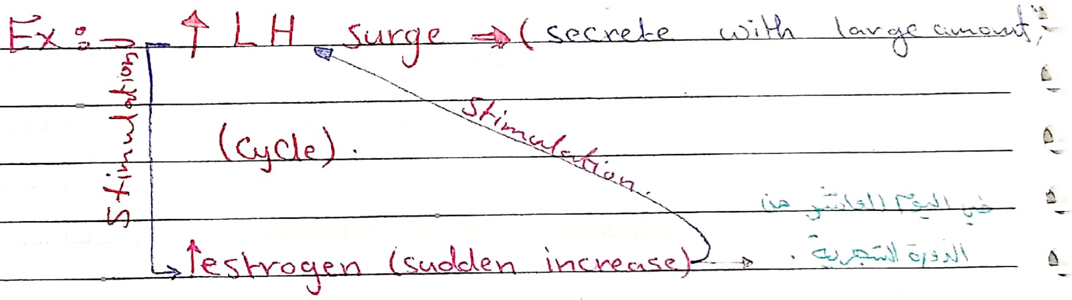
by hormone which transport from hypothalamus to ant. pituitary gland.

2- Feed back Control :-

- has relation with homeostasis.
- it's two type :-
    - a- Negative Feedback mechanism. (more common).
    - b- positive Feed back mechanism.

*** positive Feed back mechanism :-**

1- LH , estrogen (ovulation)
2 Clotting
3- hyper thermia.
4- Na^+ Channal in action potential.
5- oxytocin.
6- Shock.


Ex :-
↑ LH surge → (secrete with large amount)
Stimulation
(cycle).
Stimulation.
↑ estrogen (sudden increase)
في اليوم العاشر من الدورة الشهرية .

* الاستروجين لو ارتفع فجأة يعمل (positive Feed back) يؤدي
إلى ارتفاع الـ LH وإذا ارتفع الـ (LH) يؤدي إلى رفع
الاستروجين، وهكذا .

* لكي يحدث الـ ovulation ضروري يحدث (↑ LH surge)

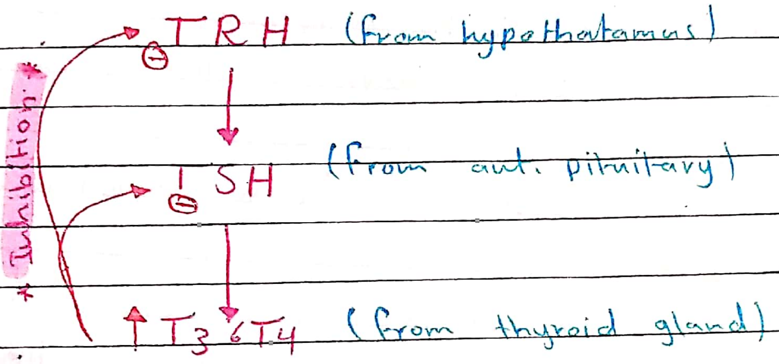
* عند استخدام حبوب منع الحمل تكون الدورة الشهرية موجودة لكن لا يحدث ovulation .
وذلك لأن الـ (LH) يكون بكمية قليلة في هذه الحالة الـ LH
يعمل Stimulation للاستروجين (والاستروجين في هذه الحالة يزداد تدريجياً وليس
فجأة) فيرجع يقلل (↓ LH) (Negative Feed back)

باختصار ↓

1- Sudden increase of estrogen → positive Feedback
→ during ovulation
2- gradually increase of estrogen → Negative Feedback
→ during oral Contraceptive.

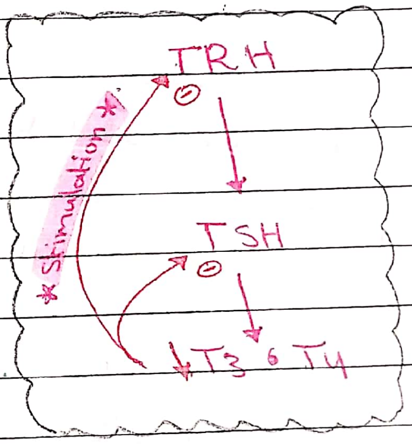
Negative Feed back mechanism

*كل الهرمونات يشتغل بيها (Negative Feed back)


TRH (From hypothalamus)
⊖
TSH (From ant. pituitary)
⊖
↑T3, T4 (from thyroid gland)
* Inhibition *

*N.B :-

1- If the relation Btw 2 hormone is Inversely (↑ T3, T4 → ↓TRH) it Called negative Feed back mechanism.


TRH
⊖
TSH
⊖
↓T3, T4
* Stimulation *

2- If the increase one hormone lead to increase other hormone (↑ LH → ↑estrogen) it Called (positive Feed back mechanism).

3- If the decrease one hormone lead to decrease other hormone → it's pathological State. → خلل في ال hypothalamus or pituitary.

Ex:- * Regulation of prolactin hormone.

1- hypothalamic control by:-

a- prolactine releasing hormone

b. prolactin inhibiting hormone (predominant)

* all hormone which secreted from hypothalamus in Balance state.

ex:- 1- Growth hormone releasing hormone
2- Growth hormone Inhibiting hormone] in Balance.

Except :-

Prolactin Inhibiting hormone (predominant)

والدليل على ذلك إنه لو انقطعت العلاقة بين الـ hypothalamus
والـ pituitary gland ← كل الهرمونات تقل ماعدا الـ prolactin
يزيد (لأنه كان في حالة Inhibition بواسطة (prolactin Inhibiting H)

2- Feed back mechanism.

الأكثر استخداما (أهمية).
وصورة أثناء الفحص في الدم أو البول يدل على الحمل

* N.B :-

* the hormones which have the similar chemical structure :-

1- Growth hormone & prolactin.
necessary ↑high Concentration to act as prolactin

2- ACTH and mylanocyte stimulating H. (MSH)

3- TSH and HCG (human Corionic gonadotropin).

(HCG)
* هرمون الحمل
يوجد في الدم والبول.
يزداد حتى الشهر الثالث
من الحمل (مرتفع جداً)
* لو كان مرتفع في الشهر الأول
ونقص في الشهر الثاني جدا
يعني أن الطفل ميت (إجهاض)
لكن لو كان بنسبة عالية
جداً في الشهر الأول ← حمل عنقودي يؤدي إلى إجهاض وعادةً ممكن يتحول إلى السـ → malignancy.

* Growth hormone Inhibiting hormone = Somatostatine.

* Growth hormone (GH) *

Somatotropin.

* it's polypeptide hormone

have the same function:
- type 1 = 191 amino acid, more than type 2
- type 2 = 176 amino acid.

* Function of Growth hormone :-

1- Stimulate Growth :-

a - in soft tissue :- it stimulate growth of all soft tissue except (CNS) ⇒ Brain.

b Cartilage and bone growth :- (indirect).

Growth hormone with Somatomedine stimulate growth of Bone and Cartilage.

* Somatomedine *.

- it's polypeptide growth factors, which secreted by the liver under effect of growth hormone.

* types :-

1- Insulin like growth Factor I :- (Somatomedin C)

- Insulin LGF I with growth hormone Stimulation Growth of Bone

والدليل إنه لو حصل نقص الـ (Insulin LGF I) ← حيعمل
عن التقزم dwarfism بالرغم من وجود الـ growth hormone
بكميات كبيرة

* GH , Cortisol & Thyroid hormone.
أهم هرمونات لها علاقة بال metabolism

2- Insulin Like growth Factor II :-

- Stimulation of growth in Fetal development. (somatomedin A)

وممكن يشتغل من الشهر الاول بعد الولادة.

* N.B:- (VIP)

- The Function of (Insulin like growth Factor I) same the Function of Growth hormone EXCept:-

IGF - I → Inhibition of lipolysis

while GH → Stimulation of lipolysis

2- Metabolic effect :-

a- protein metabolism :-

1- Stimulation of protein synthesis (anabolic hormone).

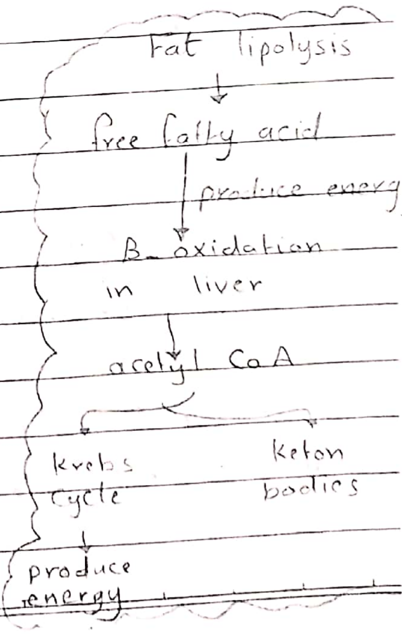
b- fat metabolism :-

1- Increase blood fatty acid

2- Stimulation of lipolysis.

أهم مصدر للطاقة

3- Inhibition of lipogenesis.


Fat lipolysis
free fatty acid
produce energy
B- oxidation in liver
acetyl CoA
krebs cycle
keton bodies
produce energy

* GH → is Diabetic genic ? why?

الموضوع :

التاريخ / / ٢٠

C- Carbohydration metabolism :-

Because → 1- Increase blood glucose by :-

a- Decrease glucose uptake by muscle (anti-insulin effect)

* anti-insulin hormone
  - → Growth hormone
  - → Cortisol
  - → adrenaline
  - → glucagon.

b- Increase hepatic output from glucose (glycogenolysis).

* N.B :-

* people with gigantism or Acromegaly (Increase growth hormone) يحصل لهم ⟹ Diabetis

* وأيضاً ارتفاع نسبة ↑ Cortisol ⇇ يسبب Diabetis

d- Electrolyte metabolism :-

↑ retention of electrolyte (for growth).

لأن النمو يحتاج الى كالسيوم و حديد ـــ إلخ.

- ↑ reabsorption. & ↓ excretion.

* N.B :-

(↓ energy) - ↓ glucose & fatty acid during fasting lead to gluconeogenesis (Synthesis of glucose from protein or fat), So ↑ GH in Child lead to ↑ glucose & fatty acid to produce energy & (prevent synthesis glucose from protein) to keep protein for growth. Called (protein spering effect)

3- lactogenic effect :-

Because it have the similar structure of prolactin. (secretion of milk).

↑ high Concentration of growth hormone lead to formation of milk in Breast

وأيضاً يكون عنه الشخص Gigantism.

4- Antiaging. effect.

↓ Growth hormone → Causes dwarfism.

↓ تظهر عليهم ملامح الشيخوخة مع إن العمر صغير.

* Regulation of Growth hormone :-

1- hypothalamic Control by

a- Growth hormone - releasing hormone.

b- Growth hormone - inhibiting hormone.

2- Feedback mechanism.

* VIP * → * Factors Stimulating Growth hormone secretion :-

(growth hormone releasing hormone).

1- ↓ Blood glucose level and free fatty acid :-

↓ Blood glucose → hypothalmus → secretion of growth hormone releasing hormone → pituitary (ant.) gland → secreted growth hormone → liver → Insuline like growth Factor I

2- Fasting and exercise :-
lead to decrease glucose in blood.

3- ↑Certain aminoacid in plasma e.g. (arginine)
له موجود بنسبة عالية في اللحوم ويعمل (Stimulation G.H)
- eat meat (Contain arginine) ⇒ Stimulation growth hormone.

4- stressful stimuli e.g :- emotions.
- Stress ⇒ ↑ Growth hormone
بالرغم من ذلك كلما تعرض الانسان لـ Stress
يحصل له (delayed growth) ! كيف؟
Because during stress the Cortisol hormone secreted in large amount Causes (protein Catabolism)

5- Going to sleep (at the beginning of normal non-Rapid eye movement seen (non-REM)
* النوم يكون مرحلتين بالبداية (non-REM) ⇐ عميق.
ومرحلة (REM) ⇐ ليس عميق ⇐ تكون أيضاً في حالة stress
* يرتفع هرمون النمو في حالة (non-REM)
* الأشخاص الحزينين تكون عندهم فترة (REM) أكثر من (non-REM)

النوم عبارة عن cycle ممكن تتكرر أكثر من مرة خلال فترة النوم.
- 80% (non-REM) ⇐ يصحى غير نشيط.
  لا تذكر فيها الأحلام (↑GH)
- 20% (REM) ⇐ يصحى نشيط.
  أذكر فيها الأحلام (↓GH)

6- Hormones: glucagons, Sex hormones. (Androgen & estrogen.)

(VIP) ⇒ * Factors inhibiting Growth hormone secretions:-

1- ↑ Blood sugar and Fatty acid.
2- During REM Sleep.
3- ↑ Blood level Cortisol
↑ Cortisol lead to ↓ GH & ↓ TSH
4- ↑ Growth hormone.
5- ↑ IGF-I in blood.
] → Negative feed back inhibition

*N.B:-

* Acromegaly → Diabetes
→ cardiomegaly (cardiomyopathy).

اللي بيكون بيسبب tumor in pituitary gland.

* post. pituitary gland *.

- it Storage 2 hormone :-
  1- ADH ⇒ from supraoptic nucleus.
  2- oxytocin. → from paraventricular nucleus

* Antidiuretic hormone * . (Vasopressin).

- poly peptide hormone.
- Consist of 9 amino acid.

* Action of ADH :⇒ (↓ urine)
  1- water retention (V_2 receptor)
  in renal (CD & late part of DCT)
  * Mechanism of action of hormone in renal :-
  1- ADH Combined with receptor of Cell membrane. (V_2 receptor) of CD
  2- Stimulation of V_2 receptor → Stimulation of Gi protein → activation of adenylyl cyclase enzyme ⇒ Convert of ATP to cAMP
  3- Cyclic AMP → ↑ permeability of CD to H_2O which lead to ↑ H_2O reabsorption.

* N.B:-
* ↑ ADH ⇒ ↓ urine.
* ↓ ADH ⇒ ↑ urine.
* in diabetic incepidus the amount of urine about (20 - 23 L/day) Because absent of ADH.

* لو نقصت السوائل بكمية قليلة لا يعمل V.C
لأن الهرمون أفرز بكمية قليلة

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2- Generalized vasoconstriction (V.C) by V_1 receptor. (by IP_3 mechanism)
* ADH to do V.C ⇒ necessary be in high concentration.
* hypovolemia (large amount) → ↑ ADH → ↑ V.C → ↑ P.R → ↑ B.P.

ضروري يكون الهرمون in high concentration.

* Factors effected in ADH *
(Control of ADH).

1- Drugs ⇒ nicotin & Morphin → Stimulation ADH
So, heavy smoker has low amount of urine.
⇒ Alcohol ⇒ Inhibition of ADH
So, the people which drink Alcohol ⇒ يكون عندهم (poly uria).

أكثر الأشخاص إدماناً للمورفين هم الجراحين

2- Stressful stimuli :- لأنها تشتغل أكثر على hypothalamus
pain, exercise, emotion, truma, and surgery ⇒ Stimulation ADH.
⇒ Cold ⇒ Inhibition ADH.

* شخص يتعاطى الكحول ومورفين ← في هذه الحالة = تأثير الكحول ← يؤثر أيضاً على cereblum.
يكون أقوى فيكون عند الشخص polyuria.

* العلاقه بين السوائل والضغط الأسموزي علاقة عكسية .

3- Osmotic pressure of plasma :- (directly).
- ↑ O.P of plasma → ↑ ADH
- ↓ O.P of plasma → ↓ ADH

4- plasma volume (ECF) : (Inversely).
- ↑ ECF volume → ↓ ADH.
- ↓ ECF volume → ↑ ADH.

- Ex :-
- hypovolemia (hypertonicity) → hypothalamus → Stimulation of osmo receptor → secrete of ADH. (↓ urine).

* N.B

Receptor has relation with pressure.

low pressure receptors
لها علاقة بال Volume
- Found in atrium, vein & pulmonary v.

* نقص أو زيادة في السوائل لا تؤثر على الضغوط يشتغل فيها Low P.R

* ↓ volume of fluid (low amount) → Low P.R → send sigle to hypothalamus → secrete ADH.

high pressure R.
لها علاقة بال pressure.
- found in ventricle & arterial (Baroreceptor).

* نقص أو زيادة في السوائل بحيث تؤثر على الضغط يشتغل فيها الاثنين ← high P.R الأثر ← low P.R

* ↑ volume of fluid (large amount) → ↑ B.P → low & high P.R (arterial) → hypothalamus → Inhibite ADH.

Oxytocin

- Polypeptide hormone.
- Consist of 9 amino acid.

*** Action of oxytocin :-**

1- Milk ejection.
by Contraction of myoepithelial cell of mammary gland.

* لو شخص انضرب عنده (thirst center)
وليس لديه أي امراض يعيش ، ولكن يحصل
له لخبطة في Urinary & GIT .
* بينما لو انضرب عند شخص يعاني من انخفاض
ADH (diabetic incepidus) يموت
الانسان لأنه يكون عنده Polyuria
ولا يستطيع تعويض الجسم بالسوائل التي
يفقدها لأنه لا يشعر بالعطش .

shima'a Mahmoud

2- Utrine Contraction. (in pregnant women).
* أثناء الولادة يحدث (dilation of cervix) فيندفع
رأس الطفل نحو ال cervix فيضغط عليه (توجد مستقبلات
في ال cervix ترسل إشارات عصبية إلى ال (hypothalamus)
يعمل على إفراز ال (oxytocin) فعندما يفرز الهرمون
يعمل (Contraction) فيدفع الطفل نحو ال cervix
فيضغط عليه (كلما ضغط رأس الطفل على cervix أكثر يؤدي
إلى إفراز الهرمون أكثر) ← Positive Feedback m.

*** N.B :-**

* من الأفضل عدم وصف إبرة الطلق عند الولادة (oxytocin).
* عند إعطاء إبرة الطلق و ال cervix لم ينفتح بعد
قد يؤدي إلى وفاه المرأه لأنه يؤدي إلى (rupture of uteruse)
* وأيضاً في حالة الإجهاض (abortion)
ممنوع إعطاء إبرة الطلق .

* in non pregnant women :-

- during sexual inter course → stimulation of gential organs in male and female → secret of oxytocin in Both ...

in Male ⇒ ejaculation of semen.

- in femal ⇒ 1- transport of sperm in femal gential tract

2- Sensation of orgasm. by Contraction of uterus

3- ejaculation of semen by contraction of vas deferens.

4- Degeneration of the Corpus luteum.

- it form after 15 day من الدورة

- Corpus luteum → endcrine organ, which secrete estrogen and progestron.

* Control of oxytocin secretion *.

1- Stressful stimuli ⇒ ↑ oxytocin.

2- Conditioned reflexes

a- need experance غريزة لأمومة عندها

b- Intact cerberal cortex ⇒ تسمع صوت طفلها يبكي

c- aquired reflex. oxytocin مباشرة يفرز هرمون

⇒ alcohol → Inhibition oxytocin.

3- Stimulation of Breast → ↑ oxytocin.

*عندما يبدأ الطفل بالرضاعة ← يعمل إفراز لهرمونين

(Sucking reflex) عن طريق ⇐ (prolactin & oxytocin)

↓ send signal to hypothalamus → secrete prolactin releasing hormone and oxytocin. → to pituitary gland → secrete prolactin.

4- Stimulation of the genital organs

↑ oxytocin.

5- Distention of cervix of the uterus.

↑ oxytocin.

* Intermediate lobe *.

- secrete mylanocyte stimulating hormone.
- it's similar to ACTH in Chemical Structure

قريب ← جدًا في التركيب الكيميائي

- MSH → bind with receptor of cell → stimulation of melanine (which responsible for pigmentation of skin).

* the Intermediate lobe atrophy in adult, so the MSH will absent, but ACTH in high concentration will do the same function of MSH. (pigmentation of skin).

* addison disease ↓ Cortisol & aldosteron بسبب مشكلة في ال adrenal gland.

Cortisol نقص

* primary addison disease (↓ Cortisol) ⇒ (negative feed back)

⇓

stimulation pituitary gland

⇓

↑ ACTH. ⇐ يعمل pigmentation of skin.

* ↓ ACTH ⇒ pale skin.

(panhypopituitarism . disease) ⇐ توقف افرازات ال pituitary

* Insulin

*it's one of the hormone which secreted from B- cell of pancreas.

* it's polypeptide hormone consist of (51 amino acid) two chain (A & B) connect to each other by C- peptide.

* When insulin (two chain) is bind with C-peptide, it will become inactive.

* importance of C-peptide :-

- to difference btw if the insulin is endogenous OR exogenous.

a- The present of C-peptide ⇒ endogenous from B-cell.

b- the absent of C-peptide ⇒ exogenous (drug).

N.B * during exercise insulin decrease due to the action of Sympathetic

* السمبثاوي العصبي يعمل تثبيط لل Insulin بشكل غير مباشر

عن طريق تحفيز ال Sympathetic ← (↓ Insulin)

* glucose transport *.

- it's two type of transport :-

1- Sodium dependent (SGLUT) active transport (secondary active transport).

*glucose enter to all Cell of Body.

* Insulin not enter (act) to all cell of Body.

2- Sodium Independent (GLUT)

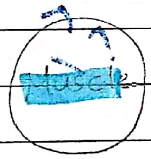
- it's 7 type.
- Facilitated transport (need Carrier).
- the Insulin not act in all cell of body but found mostly in Muscle and adipose tissue

* GLUT 4 :→ كلما زاد

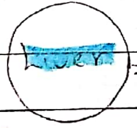
- The only transport (Carrier) which depend on Insulin.

عددها
زادت
كمية الأنسولين
الداخلة
للخلية

*. Insulin act mainly on Muscle cell and adipose tissue, that's why large amount of glucose storage in muscle and adipose tissue.



→ Contain GLUT 4
(more glucose will enter).



⇒ Contain no GLUT 4 (Contain GLUT 2 & 7)
(less glucose will enter).

*وجود الأنسولين يؤدي الى زيادة كمية الجلوكوز الداخلة للخلايا.
لأنه يسهل دخول الجلوكوز للخلية. (لكنه ليس السبب الرئيسي لدخول الجلوكوز دائماً)

* B-cell :→ insulin not act on it.
- Contain GLUT 2

* أحد أسبابه افرازها للأنسولين هو دخول الجلوكوز للخلية.

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* مرضى السكر يكون عندهم نقص فيا الوزن

* أحدى علامات الـ Malignant Cancer هو فقدان الوزن.

* Mechanism of action *.

1- Insulin is polypeptide hormone, So it bind with receptor in the cell membrane.

2- it's receptor → 2 α Chain → extracellular
→ 2 β Chain → intracellular.

3- When hormone bind with receptor (α chain) it lead to increase tyrosine-kinase activity Which found in the β Chain due to stimulation of β.

4- Increase tyrosine activity lead to phosphorylation of protein and dephosphorylation of other ~~hormone~~ protein. → this lead to do action of insulin.

* Action of insulin hormone *

1- Maintain blood glucose homeostasis.

2- effected of insulin in Carbohydrate :- By

a- facilitated of transport of glucose to Muscle and adipose tissue by GLUT 4.

b- Facilitated diffuse of glucose to Liver

- Glucose enter the liver by $GLUT_2$ and inside The liver, There's two type of glucose: (1- Free glucose and 2- glucose 6-phosphate), So the free glucose Convert to glucose 6-phosphate (by hixo-kinase) (glucose kinase)

الذي يحفزه هو الانسولين.

→ This lead to decrease glucose inside the liver which lead diffuse glucose from high Concentration (Blood) to low Concentration (liver) in large amount.

c- Stimulation of glycogen synthetase enzyme
: Convert of glucose to glycogen).

d- Inhibition glycogenlysis and glyconeogenesis.

3- effect on protein metabolism.
« anabolic effect by increase uptake of amino acid by liver and ↓ gluconeogensis »
"Insulin is 4th hormone for growth"

4- effect on lipid metabolism
" Stimulation of lipogensis and inhibition of ketogensis and inhibition of lipolysis"
« ↓ decrease Insuline ⟹ lead to lipolysis »
(↓ decrease Body wieght)

5- Important of insulin for Some electrolyte.
- in hyperkalamia ⇒ Insulin used to stimulate K^+ influx to the cell.
« also use glucose to prevent hypoglycemia »

* Regulation of insulin hormone :-

- by Feed back Mechanism (positive)
(No hypothalamic regulation).
↑ glucose ⇒ ↑ Insulin

* Factors that increase Insulin :- (stimulation).

1- hyperglycemia :→
- the glucose enter to B-cell by $GLUT_2$, this lead to glycolysis of glucose to produce energy. (ATP) → this energy lead to close K^+ channal which lead to increase K^+ inside the cell which lead to depolarization of cell.
the depolarization lead to open Ca^{+2} channal lead to influx of Ca^{+2} from extracellular.
- the Ca^+ bind with insulin viscle in B-cell lead to rupture & release Insulin from visecle by exocytosis.

* كلما كان دخول الجلوكوز بكميات كبيرة ، كان خروج الانسولين بكميات كبيرة .

* العلاجات التي تنقص الانسولين ← تعمل على فتح قنوات البوتاسيوم ← خاصة في حالة لاتفرز الانسولين

2- Increase amino acid :-
Ex: arginine.

3- glucagon.

4- Parasympathetic

5- oral hypoglycemic drug.

عددها ⇐ 6- gastrointestinal hormone.
أكثر من 30
Ex: gastrin, secretin, cholycystokinane

7- keton bodies.

* Factors that decrease Insulin (Inhibition) :-

1- hypoglycemia (fasting)
2- Somatostatine ⇒ (Inhibition for Insulin and glucagon).
3- Sympathetic
4- toxic substance. ⇒ (Alloxan) ⇒ very toxic
لـ تستخدم لتدمير خلايا B ← تستخدم في التجارب
بالبداية يسبب hypoglycemia ثم بعدها
(باليوم الثاني) تسبب Diabetes.
5- ↓ decreas potassium.
6- B- Blockers.
7- durg stimulated α_2 receptor.

* effect of Insulin deficiency *.

1- hyperglycemia.
2- Glucosuria.
3- poly uria.
4- polydipsia and polyphagia.
5- weight loss
6- ↑ Cholestrol. (Because lipolysis).

Thyroid hormone.

* Thyroid gland lies infront the neck under larynx. (in each side of trachea)

* it Consists of two lobe

* Thyroid gland Consist of follicles
  → 1- lined by epithelial cells
  → 2- filled with Colloid. ⇒ protein materials.

* it Contain also parafollicular cell (c-cell) (Clear cell). ⇒ which secrete Calcitonin.

* the follicular cell :-

Inactive	*active.*
- large follicle	- Small follicle
- flat epith.	- Culomnar epith.
- large amount of Colloid.	- Small amount of Colloid.

*Thyroid hormone :-

1- Thyroxin (Tetraiodothyronine) T_4 (80%)
2- Triiodo thyronine T_3.
3- Reverse T_3 (RT_3)
4- Calcitonin ↓ Ca^{+2} in blood

*Mechanism of Action :-

مذكور مسبقاً

* Action of thyroid hormone :-

1- Calorigenic effect :-

- ↑ Metabolism → ↑ O_2 Consumption → ↑ heat production → ↑ Body temperature..

*Calorigenic effect :-
1- Thyroid
2- glucagon
3- Adrenaline
4- Cortisol (permassive)

- this effect occur in all tissue Except :-

1- adult Brain.
2- Uterus
3- Testes why?

- Because it lead to decrease Spermatogenisis (OR lead to Infertility due to damage of semniferus tubule).

* N.B :-

* The thyroxin in adult Brain can't does metabolism (Calorigenic effect), But it does other Function

- hyper thyrodism → Intolarance of heat.

- hypothyrodism → دائماً يشعر ببرودة حتى في الأيام الحارة (الصيف).

*Thyroid, Adrenaline & glucagon.
(↑ Contractility.

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2- Effects on the heart :-

- ↑ Contractility (S.V) →
& ↑ H.R by:- 1- Direct stimulation of S.A.N.
2- ↑ increase metabolism.
3- increase respons of heart to Catecholamine.
→ & ↑ C.O → ↑ Blood pressure.

- hyper thyrodism → tachy Cardia, hypertension
OR extrasystole

N.B * extrasystole
نبضة قوية.

→ physiological (stress & المنبهات).
→ pathological → Cardiac disease.
→ Irritable bowel syndrom. ← * القولون العصبي.

الأدوية المنبهة
ضارة جداً (لا توصف)

- hypothyrodism → Brady Cardia and hypotension
ماعدا في حالة واحدة يحصل عند الشخص hypertension
* وهي عندما تكون الشخص مصاب ب atherosclerosis (hypercholestrolemia).
تأتي بعد مضاعفات
وبعد فترة طويلة
من الـ hypothyrodism

c- sexual growth :-

in male :- for spermatogenesis (with unknown function).

- in female :- for menstrual cycle (with unknown function). & Milk secretion during lactation.

- hypothyrodism :→ Infertility in male
→ amenorrhea

أو انقطاع الدورة الشهرية.

* N.B :- important :-

* بعض الأطفال يكون عندهم نقص بال thyroid hormone
لكن بكمية قليلة تؤدي إلى :-

1- delayed in growth.

2- تأخر ظهور الأسنان

وتأخر المشي

* لكن بعض الأطفال لا يوجد عندهم هرمون (thyroid)
وتكون أعراضه :- (Called cretinism)

1- eye swollen

2- nose is depressed.

3- tongele is enlarged.

4- umbilical hernia.

5- Mental retardation. (M.R)

من الضروري عمل فحص للهرمونات الدرقية عند ولادة الأطفال.

تكون الأعراض واضحة جدًا وضروري معالجة الطفل خلال (6 - 3 أشهر) إذا لم يتم علاجه فإنه يصاب M.R لا يُعالج بعدها.

* إذا أُصيب شخص بالغ بنقص هرمون الدرقية
فإنهُ لا يصاب بـ (Mental retardation) لكن يصاب
بأعراض الـ hypothyrodism :ـ

1- Intolerance to Cold
2- hypotension & Brady Cardia.
3- loss appetites.
4- increase Body wieght
5- increase Cholesterol.
6- loss of Concentration.
7- Conistabition & fatigue.
8. خمول & زيادة في النوم.

4- effect on respiratory System :-

- it Causes increase respiratory rate (depth & Frequancy) due to increase metabolism.
- Increase the amount of $\boxed{2,3\ DPG}$ in RBC.

$\downarrow$ shifting to Right (decrease affinity Btw O_2 & H.b) Causes release O_2 in large amount which important in metabolism.

the Factors which lead to shifting to left Causes hypoxia.

مهم جداً (شفوي)

5- protein metabolism :-

- Normal level of thyroid hormones stimulate protein synthesis and growth.
- Increase thyroid hormone causes protein catabolism.

*** N.B :-**

- hyperthyrodism → catabolism in bone → release Ca^{+2} → osteoprosis.

* hyperthyrodism
* hyper parathyrodism
* Cushion syndrome (↑ cortisol)
] → osteoprosis with large Ca^{+2} in blood.

Causes ← Spontaneous fracture.

بسبب سحب كمية كبيره من Ca^{+2} من العظام.

6- Carbohydrate metabolism :-

a- increase uptake and utilization by the tissue (↓ glucose)
b- Insulin hormone secretion (↓ glucose)
c- Liver glycogenolysis (↑ glucose)
d- Gluconeogenesis (↑ glucose)
e- Intestinal absorption of glucose. (↑ glucose).

معدل * LDL = 100 -130 mg ⇒ Bad Cholestrol

بالتمارين . * HDL = 35 - 65 mg ⇒ good Cholestrol

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يزيد بالتمارين

* during Normal thyroid ⇒ Balance . (nor decrease either Increase of glucose).

* But during hyperthyrodism ⇒ hyperglycemia . due to potentiate anti . insulin hormone :-

- → Catecholamine.
- → Glucagons.
- → Cortisol
- → Growth hormone.

7- Lipid metabolism :-

a- Thyroid hormone ⇒ ↓ Blood Cholestrol level due to increase number of LDL receptor in liver. ⇒ increase uptake of LDL to Liver ⇒ degenaration of LDL in liver.

b- Stimulation of lipolysis. (↓ lipid)

* hypothyrodism :- ⇒ hyperCholestrolemia. (LDL)

* hyperthyrodism :⇒ hypoCholestrolemia. (LDL).

8- Vitamin metabolism :-

- Thyroid hormone are necessary for hepatic Conversion of Carotene to Vitamin A.

موجود في الجزر . مهم في الرؤية الليلية

لذلك نقصه يسبب عشى ليلي .

* ↑ vitamin A ⇒ Causes تظهر هذه أعراض نفس أعراض
headache ← (tumor in Brain) شخص عنده
projectile vomiting , حول ,
& without nausea.

* hypothyrodism ⇒ ↑ Carotene
(Carotenemia yellowish)
- yellowish in all body except sclera of eye.

9- Gastrointestinal tract:-

- Thyroid hormone increase motility, secretion
appetite and absorption.

بياكل ⇐ * hyperthyrodism: ↑ appetite , thin
الـ parasympathetic & causes diarrhea.
يؤدي لمغص , إسهال

* hypothyrodism: ↓ appetite , obese
& Causes Constipation.

10- Haemopoietic System:- (Blood)

a- Thyroid hormone stimulate:
1- erythropoiesis (thyroxin, erythroptine, endrogen)
2- ↑ absorption of B_{12} , iron & folic acid.

11- potentiate the anti-insulin hormone:-
a- Catecholamine.
b. Glucagons.
C- Cortisol
d- Growth hormone.

12- Calcitonin hormone ⇒ ↓ Ca^{+2} in Blood.

13- reverse T_3 ⇒ Storage.

* Regulation of thyroid hormones :-
1- Thyroid stimulating hormone. (TSH).
2- Dietary iodine intake.

* First :- Dietary iodine intake :-
* need 150 microgram per day.
* An adequate dietary iodine intake is essential for normal thyroid function.

* Causes of hyperterophy of thyroid gland:-

* hypothalamus $\xrightarrow{TRH}$ Ant. pituitary gland $\xrightarrow{TSH}$
thyroid gland ⟶ T_4, T_3

But if the iodine is inadequate
it Causes Negetive Feed back

- the Negative Feed back

aut. Pituitary gland → Excess TSH

⇒ thyroid gland (hypertrophy) (goiter).

*So, ↓ Iodine ⇒ ↓ T_3 & T_4.

* ↑ Iodine in large amount lead to ↓ decrease Thyroid hormone by (Wolff - Chaikoff effect).

due to :-

1- prevent bind of iodine with tyrosine.
2- make thyroid gland un respons to TSH.
3- Inhibition of proteolysis enzyme of thyroglobulin.

*N.B :

*إذا شخص عنده (hyperactivity) (hyper vascularty) للغده الدرقيه
لا نعمل للشخص عملية لأنه قد يؤدي إلى الـ Bleeding .
* لذلك نعطي المريض (Iodine) بكميات كبيره
لكي تقلل الـ (vascularty & activity) للغده الدرقية .

* كل الهرمونات [illegible] تفرز من [illegible] and pituitary [illegible]

لها نوعين من الـ regulation :-

1- hypothalamic regulation.

* Second :- thyroid stimulating hormone. (TSH).

* Factors that Control TSH secretion :-

1- Thyrotropin releasing hormone. (TRH).

↑ TRH → pituitary gland → ↑ TSH → Thyroid gland → ↑ T_3 & T_4

2- Feed back mechanism (Negative) :-

- ↑ T_3 & T_4 lead to negative feed back inhibition for Hypothalamus OR pituitary gland.

* other Factors control TSH secretion :-

1- Cortisol (glucocorticoids), Dopamin (prolactin inhibiting hormone) and Somatostatin (Growth hormone inhibiting hormone) inhibite TSH secretion.
lead to (↓ T_4 & T_3).

2- CirCardian rhythm (durinal variation).
- ↑ secretion at night (منتصف الليل)

3- ↑ HCG in high Concentration act as TSH.

* بعض النساء أثناء الحمل يحصل عندها goiter & hyperthyradism

Because ↑ HCG in high Concentration lead to activate the thyroid receptor lead to ↑ T_3 & T_4 (hyperthyradism) & goiter.

* أيضاً زيادة HCG في فترة الحمل يسبب (vomiting).

Adrenal gland ⇒ مهمة جداً

* also called suprarenal gland.

Adrenal gland

outer cortex 72%.
(aldosteron, Cortisol & androgen)

→ outer layer:-
Called Zona glomerulosa.
(Secrete aldosteron)

→ Middle layer :- (largest).
Called Zona Fasciculata.
(Secrete → Cortisol 90%.
↳ androgen. 10%.

→ inner layer:-
Called Zona reticularis.
secrete → androgen. 90%.
↳ Cortisol 10%.

inner medulla. (28%)
(Catacholamine hormones).
→ adrenaline
→ noradrenaline
→ Dopamine.

The adrenal Cortex Contain large amount of 1- Mitochondria.
2- Smooth endopalsmic R.
in which steroid hormone biosynthesis take place.

*** N.B:-**

لانستخدم ال Cortisol & مشتقاته
كعلاج للمريض في أي حالة لأن له أعراض جانبية كثيرة وخطيرة
منها :-

1. osteoprosis.
2. D.M
3. hypertension.
4. peptic ulcer.

ممكن يؤدي إلى الـ
immune spression
إذا كان بجرع كبيره

*أي هرمون يعمل (protein Catabolism) ⇐ يسبب osteoprosis.

*هناك أمراض ممكن نعطي المريض الـ Cortisol كعلاج منها:

1- Autoimmune disease.
2- severe Bronchial asthma.
3- Severe arthritis.
4- during trans plantation. ⇐ في هذه الحالة نضع المريض في غرفة معقمة 100% وذلك لأن أبسط ميكروب يؤدي إلى الإصابة infection بسبب نقص lymphocyte
5- malegnancy (في بدايه مراحلة).

* Cortisol (glucoCorticoids) *

* Action of glucoCorticoids (Cortisol) :-

1- Metabolic effect :-

a- protein metabolism :-

1- In extrahepatic tissue :-
- occur protein Catabolism. to amino acid.
- ↓ uptake of amino acid by tissue Except liver.

ex:- osteoporosis due to Catabolism of protein which lead to release Ca^{+2} in Bone to blood.

Ca^{+2} = 1100gm
99% in Bone
1% in Body fluid

- In hepatic tissue :-
- increase uptake of amino acid from blood to liver & Conversion into → protein. by protein synthesis.
→ Carbohydrate by gluconeogenesis.

explain :-
why Cushion s
Cause osteoporo
B/c Catabolism of

b- Carbohydrate metabolism :-

it Causes hyperglycemic effect due to :→

Cause D.M ←

1- Stimulation of gluconeogenesis (most import.)

2- Anti-insulin effect :-

by decrease glucose uptake by tissue through inhibiting the hexokinase enzyme.

3- Activation of glucose 6-phosphatase :-

* glucose 6-phosphate $\xrightarrow{\text{g-6-phosphatase}}$ glucose + pi

glucose will release to blood.

c- Fat metabolism :-

1- lipolysis :-

- to use fatty acid for source of energy.

Causes

2- lipaemia :-

- Increase fatty acid in Blood.

Causes

3- Ketogenesis :-

- Formation of keton bodies in liver.

Causes

4- Ketosis :-

- Increase keton bodies in blood

في المعدل الطبيعي يحل ← 5- Deposition of fat :-

- in high Concentration Causes abnormal distribution of fat :-

normal Distribution of fat in body

a- buaffalo hump :- in cervical (Back)

(Cushion syndrom لـ كيس دهني مثل السنام (يكون عند الشخص

b- moon face.

c- central obesity.

* N.B :-

* in Diabetic ketoacidosis (DKA) :-

↓ Insulin in large amount OR absent of Insulin lead to stimulate (lipolysis) → ↑ fatty acid → ↑ keton bodies

عبارة عن acid

→ Causes acidosis

قد يدخل المريض في Coma

* Use Cortisol as drug (exogenous)

← في هذه الحالة إذا بدأ ظهور الأعراض الجانبية للعلاج

فإننا لا نوقف العلاج مباشرة (فجأة) وإنما تدريجياً.

لأن استخدام الكورتيزول (exogenous) يعمل (Inhibition)

لل ACTH ⇐ مما يؤدي إلى (Atrophy) ⇐ للغدة الكظرية.

فعندما نوقفه فجأة يدخل المريض في (Addison craisi)

→ Which may lead hypovolemic shock

← وقد يتوفى الإنسان لذلك إذا حدث لشخص هذا المرض نعطيه

مباشرة ونعطيه (I.V fluid) ← in both side

2- Water and electrolyte Balance :-

a- in water :-

in normal level ⇒ diuretic action due to :-

1- Inhibition of ADH.

(↓ of permeability of renal tubule to H_2O).

2- Stimulation of GFR.

3- Stimulation of ANP.

Catabolism of prot

* Metabolic action of Cortisol :-
(lipid, protine, Carbohydrate, water, and electrolytes).

b- Electrolyte metabolism :-

- in normal level act as aldosteron
(weak activity).
- in high Concentration (Cushion Syndrome)
it act as aldosteron (Strong effect)

Water & Solute retention:
- a- ↑ Na^+
- b- ↓ K^+
- c- ↑ ECF volume.

Cause hypertension

3- effect in Blood cell and lymphatic tissue :-

- ↑ neutrophil, ↑ RBCs & ↑ platelets
(in small amount).
- ↓ eosinophil & ↓ Basophil. (small amount).
- the very important Function of Cortisol
in Blood is ↓ lymphocyte.
So, it Called immunosupression drug.

لذلك يستخدم في حالة (organ transplantation)
لتقليل المناعة حتى لا يتم رفض الجسم للعضو الذي تم زراعته
في هذه الحالة يوضع المريض في غرفة معقمة 100 ٪ لأنه
أسهل ما يكون ممكن يسبب للمريض Infection.

4- Anti-inflammatory effect :-

- Cortisol in large dose inhibit inflammation reaction B/c it inhibiting release of lysosomal enzymes by stabilizing membrane of lysosomes.

5- Anti-allergic effect :-

- Cortisol in large dose prevent release of histamine (New) from the mast cell.

- histaminase enzyme Break down of histamine which found in the Blood.

*ارتفاع ا histamine بالجسم بشكل كبير يعمل ١-

1- allergy
2- V.D ⇒ hypotension
& may Causes anaphlactic shock.

[illegible] ← 6- Resistance to Stress :-

- Cortisol increase the body resistance to stress by :-

a- Increase glucose & use it source of energy by:-
1- Anti-insulin effect.
2- Stimulation gluconeogenesis.
3- Activation of glucose-6-phosphatase.

b- Increase fatty acid as source of energy by:-
1- Stimulation of lipolysis

c- Increase response to catecholamine.

d- Inhibition the formation of prostacyclin (prostaglindin I_2).

عشان يحصل ارتفاع في الضغط ويمنع هبوط الضغط

7- permissive action :-

- Cortisol are important for helping other hormones to perform their action:-

مهم جدا

a- glucagon hormone :-
in (gluconeogenesis & calorigenic effect)

b- Catecholamines hormone :-
in (V.C , lipolytic , Calorigenic and bronchodilator).

8- effect on other hormones :-

- Cortisol decrease the secretion of Growth hormone and TSH.

9- effect on the respiratory system :-

- During fetal life, the Cortisol accelerate the formation of surfactant in lung.

(R.D.S) اذا نقص عند الاطفال حديثي الولادة * (Surfactant)

Collaps Pulmonary edema.

10- other action of glucocorticoids :-

a- Increase appetite.

b- Stimulation of gastric HCl and pepsin secretion. (Cause peptic ulcer).

c- Increase excitability of Brain cell.

*gastric Juice :-

1- HCl

2- pepsin

3- IF

4- Mucus.

* N.B :-

* Why Cushion syndrome Causes D.M ?

* Why Cushion syndrome Causes osteoporosis ?

* Why Cushion syndrome Causes hypertension ?

* Why Cushion syndrome Causes peptic ulcer ?

(Cortex)

* الهرمون الوحيد الذي يؤثر مباشرة على (Adrenal gland) هو ACTH

- hypothalamus → ↑CRH → ant. pituitary gland →
↑ ACTH → Adrenal gland → ↑Cortisol (large)
→ ↑Aldosteron (less)

لأن تأثير ACTH على (Zona glomerulosa) بسيط

* **Factor Control of ACTH secretion :-**

1- CRH (hypothalamic regulation).

2- feed back mechanism (↑ Cortisol in blood lead to inhibition of → hypothalamus
→ ant. pitiutary.

3- stressful Stimuli.

* ال Stress يؤثر على ال hypothalamus وأحيانا
يؤثر على ال higher brian center والذي بدوره يؤثر على
ال hypothalamus

stimulation of hypothalamus → ↑CRH
→ pituitary gland → ↑ ACTH → Adrenal gland → ↑ Cortisol.

4- Circadian rhythm.

* increase secretion during early morning which give for body activity. B/c it increase Brian cell excitiblity.

* ماهو الذي يجعل الـ Brain في حالة excitation
(يقظة مستمرة) ؟

- Acending reticular activiting system.
(ARAS).

* عندما يحصل (Inhibition for ARAS) ⇐ ينام الإنسان

* في حالة حدوث (Cut for ARAS) ⇐ يدخل الإنسان
في حالة Prolonged sleep

Shimaa* Mahmoud

* Shimaa Mahmoud Ali Ahmed Handhal *

NOTICE

* Calorigenic effect :-
1- Thyroid
2- glucagon.
3- Adrenaline
4- Cortisol (permassive)

* anti-insulin hormone :-
1- Catecholamine
2- glucagons
3- Cortisol
4- Growth hormone.

* hormone has related with growth :-
1- Growth hormone
2- thyroid hormone.
3- sex hormone.
4- Insuline.
5- Cortisol.

NOTICE

*اهم هرمون ينظم البوتاسيوم هو الالدوستيرون .

* Aldosterone * .

* action of aldosterone :-

1- ↑ Na^+ in the blood.
2- ↓ K^+ in the blood.
3- ↑ ECF volume.

* site of action of aldosterone :-

1- in The Kidney
(late part of DCT and CCD).
- Mechanism of action of aldosteron in the kidney. مذكوره سابقا .

2- in Sweat gland , Salivary gland :-
- ↑ Na^+ reabsorption by the duct of the secreting gland.

* في المناطق الحارة يحصل تعرق زيادة ⇐ يفرز الجسم الـ aldosterone
لكي ينقص الاملاح من الـ Sweat ⇐ فيكون اغلب الـ Sweat ⇐ ماء.
- لأنه لو ما حصل امتصاص للاملاح من الـ Sweat يحصل للانسان
hyponetremia ⇐ بسبب خروج Na^+ مع الـ Sweat بكميات كبيرة .

3- in the GIT :-
- increase Na^+ absorption in small intestine , and increase K^+ secretion in large intestine.

* Regulation of aldosterone :-

(Factors that effect in aldosterone).

1- Renin - Angiotensin system.

(hypovolemia) during hypotension → renal ischemia → Stimulation for Renin which convert the angiotensinogen to Angiotensin I → Angiotensin I convert to Angiotensin II by ACE. → Angiotensin II → V.C
→ ↑aldosteron.

* Factors stimulate renin secretion:-

1- Renal ischaemia :- during:
a- Renal artery stenosis.
b- hypotension caused by hypovolaemia.

3- prostaglandine
4- ↓NaCl in macula densa. ⇐

2- Renal sympathetic nerve stimulation :-
sympathetic ⇒ ↑Renin secretion.

* Factors inhibite renin secretion :-

1- Feed back mechanism :
↑ aldosteron secretion → ↑ Na^+ & water retention → hypervolaemia (↑ ECF volume) → Inhibition of renin secretion.

2- Angiotensin II has a direct inhibitory effect on renin secretion.

K = 3.5 – 5 mmol

Na = 135 - 145 mmol

Ca = 9 - 11 mg.

بكميات قليلة

2- ACTH. ↑ * يفرز كورتيزول بكميات كبيره والدوستيرون

- has permissive effect on aldosteron secretion.

3- Na^+ and K^+ Concentration in plasma :-

- aldosterone secretion is inversely proportional to Na^+ level.

($\downarrow Na^+ \Rightarrow \uparrow$ aldosterone).

- aldosterone secretion is directly proportional to K^+ level.

($\uparrow K^+ \Rightarrow \uparrow$ aldosterone).

* in $\uparrow K^+$ → direct stimulation of Zone glomerulosa ⇒ secretion of aldosterone ⇒ $\downarrow K^+$.

* in $\downarrow Na^+$ ⇒ hypovolemia ⇒ renal ischemia ⇒ stimulation Renin → V.C

↳ stimulation of aldosterone (indirect by Renin).

4- ANP :-

- inhibition of Renin.
- ↑ Na^+ excretion by Block of aldosterone.

5- Circadian rhythm :-

↑ aldosterone secretion in early morning & decrease at night.

* Ca^{+2} and ph^{-2} metabolism *

* Function of Ca^{+2} :-

1- Muscle Contraction.
2- Bone and teeth Formation.
3- Blood Coagulation (Factor IV).
4- second messenger. (Calmodulin System).

* The hormone which has relation with Ca^{+2} metabolism :-

1- parathyroid hormone.
2- Active form of vit. D_3.
3- Calcitonin

① parathyroid hormone (Action) :-

a- increase Ca^{+2} in the blood.
b- decreas PO_4^{-3} in the blood.

* $Ca^{+2} \times PO_4^{-3}$ = Constant.

So, in normal person ↑ Ca^{+2} lead to ↓ PO_4^{-3} والعكس .

* زيادة الـ Ca في الدم يؤدي الى خروجه مع البول (calciuria).
ويكون عرضه لل stone بكمية كبيرة

* Mechanism of action of parathyroid hormone :- (protein hormone).

1- Bind with receptor in cell membrane to form hormone receptor complex.

2- activation for receptor lead to stimulation of G-protein. (α, β, γ)

3- the α subunit bind with Adenylyl cyclase.

4- Adenylyl cyclase with convert the ATP to cAMP.

5- the formation of cAMP (2nd messenger) lead to cell response.

← تذكر مع الوظائف.

* How the parathyroid hormone ↑ Ca^{+2} in Blood ?

1- Stimulation of osteoclast (Bone eating cell). lead to release Ca^{+2}. from bone to Blood.

2- ↑ reabsorption of Ca^{+2}. in late part of DCT under effect of parathyroid hormone.

*ال Ca^{+2} & PO_4^{-3} ضروري تكون في حالة normal
لأنها لو نقصت أو زادت خطر على القلب.

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*

3- increase absorption of Ca^{+2} in small intestine (by indirect mechanism).
by Active form of vit. D3 which parathyroid hormone help in formation of it.

* أغلب حالات + Cancer
بتكون فيها ($\uparrow Ca^{+2}$)

*How parathyroid hormone ↓ PO_4^{-3} in Blood ?

1- decrease reabsorption of PO_4^{-3} in PCT.

2- Calcitonin hormone :-
- secrete from parafollicular cell, (clear) (C) cell of thyroid gland.
($\downarrow Ca^{+2}$ in Blood ⇒ Deposition in Bone)

*Action :-
1- ↓ Ca^{+2} in the blood. by :-
a- Inhibition of osteoclast & stimulation of osteoblast. in Bone
b- Inhibition of reabsorption of Ca^{+2}, PO_4^{-3} in late part of DCT. in kidney
(↑ exeretion)
c- Inhibition absorption of Ca^{+2} & PO_4^{-3} in small intestine.

* ↑ Calcitonin :-

1- in Children for growth.
2 in pregnant.
3- in lactating women.

* Why in pregnant women ↑ Calcitonin ?

لأن في هذه الحالة يتم استهلاك الـ Ca^{+2} بكميات كبيره
واستهلاك Ca^{+2} يؤدي إلى تحفيز الـ parathyroid H. يعمل
على سحب الـ Ca^{+2} من الـ Bone إلى الدم فيؤدي إلى (osteoporosis)
ولذلك زيادة الـ Calcitonin يمنع حدوث هذا الشيء في المرأة الحامل
بحيث يعمل على منع خروج Ca^{+2} من العظام ليحمي العظام من الهشاشة
وهنا تعوض المرأة (exogenous Ca^{+2}).

- أثناء الحمل يرتفع هرمون الاستروجين بحيث يعمل تحفيز أفراز
الـ Calcitonin بكميات كبيرة.

ممكن نضيف علاج Ca^{+2} للمرأة الحامل ويكون من الشهر الثاني.

*N.B * (↓ Ca^{+2} $\xrightarrow{\text{Negative Feed back Mechanism.}}$ Stimulation of Parathyroid. hormone.

*N.B * → ↑ Parathyroid ⇒ lead to osteoprosis.
↳ ↑ Calcitonin ⇒ lead to stronge bone.

Sunlight ⇒ in skin

* Formation of active Form of vit. D_3 *.

3- active form of vit. D_3 :- (Action)

1- increase Ca^{+2} & PO_4^{-3} in Blood
by increase absorption from small
intestine. (by increase synthesis
of Calbindin D protein).

2- increase reabsorption of Ca^{+2}
in late part of DCT.

3- in normal level stimulation of
osteoblast. (development of Bone by osteoblast.
(↑ Vit. D_3 ⇒ lead to release Ca^{+2} from
bone (osteoprosis).

4- Mobilization of Ca^{+2} & PO_4^{-3} from
bone (in high Concentration).
(stimulation of osteoclast)

5- Stimulation of lymphocyte.
(↓ Vit. D_3 ⇒ lead to recurrent infection)

* Control of Vit. D_3 :-
by Controlling of 1α hydroxlyase
* ↑ 1.α hydroxylase ⇒ ↑ active form of
vit. D_3.

* Note :-

* ↓ Vit. D_3 → Causes recurrent infection in childern.

* نقص فيتامين D في الاطفال بسبب الكساح بسبب نقص Ca^{+2}

* اذا كان شخص يعاني من نقص فيتامين D نعطيه جرع وبعد شهر نفحص نسبته ، وإذا كان أعلى من النسبة المطلوبة نوقف العلاج لأنه يقوم بعكس عمله ويسبب هشاشة عظام

* Type of lymphocytes :-

1- T- lymphocyte.
2- B- lymphocyte.
3- Non B- Non T (Called Neutral killer cell)

* Type of T-lymphocyte :-

1- helper. ⇒ immune. تنظم الـ
2- cytotoxic

*فيروس الايدز يضرب ال
helper 1, 2
T- lympho cyte.

** half life (5-10 min).

glucagon

- it's polypeptide hormone Consisting of 29 amino acid , have molecular weight 3485

- it secreted by α- cell of pancreatic islets.

- Called hyperglycemic hormone.

* Action of hormone :-

in normal level of hormone. ←

1- Increase blood sugar (hyperglycemia). due to increase output of glucose from Liver by
   → stimulation of glycogenolysis
   → // // gluconeogenesis.

2- Increase lipolysis in adipose tissue (lipolysis & Ketogenesis).

3- Calorigenic action due to increase hepatic deamination of amino acids.

4- Increase Contractility of heart (positive entropic).

5- Stimulation secretion of growth hormone, Insulin and pancreatic Somatostatin.

6- Inhibition Gastric secretion.

7- Increase Bile secretion.

8- Increase Blood flow to Some tissue especially the kidney

*N.B :-

- The glucagon hormone does function (Action) No. 2, 3, 4, 5, 6, 7, 8, 9 within high Concentration (No physiological dose).

* Regulation of glucagon hormone *.

1- Factors that increase glucagon :-

1 a- during hypoglycemia.
2 b- Certain amino acid ex: alanine.
3 c- Certain GIT hormone ex: CCK & gastrin.
4 d- Cortisol hormone.
5 e- Sympathetic ex: exercise, Stress, starvation.
6 f- para Sympathetic ex: vagal tone, acetycholine.
7 g- drug → theophylline. ⇒ for asthma.
→ B adrenegic receptor Stimulator.

2- Factors that decrease glucagon :-

1 a- hyperglycemia.

- GABA (gamma-aminobutyric acid) from B-cell (together with insulin) inhibite α-cell.

2 b- Somatostatin and insulin.

3 c- Certain GIT hormone ex: Secretin → Secret from S-cell.

4 d- drugs
  - → α-adrenergic receptor stimulator.
  - → Phenytoin ⇒ for epilepsy

5 e- Increase free fatty acid and ketone Bodies Except in DKA the glucagon secretion is not inhibition.